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Case Report

Pregnancy after neoadjuvant chemotherapy followed by abdominal radical trachelectomy in stage IB2 cervical cancer: A case report

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Introduction

Recently, uterine cervical cancer in the young generation has been increasing in Japan. Since Japanese females have tended to marry later in life during the past several decades, it is not rare that cervical cancer patients require radical trachelectomy (RT) to retain fertility. Since D'Argent et al. performed the first vaginal radical trachelectomy (VRT) in 1987, this procedure has become widespread throughout the world. Due to the narrow vaginal anatomy of Japanese women, abdominal radical trachelectomy (ART) has been performed in most cases (74.7%, 201/269) in Japan (Sato et al., 2011). RT has been adapted for patients with stage Ia1-Ib1 cancer, and neoadjuvant chemotherapy followed by VRT has been attempted for larger tumors (Marchiole et al., 2011; Gottschalk et al., 2011).

In this report, a patient with stage Ib2 squamous carcinoma was treated with neoadjuvant intra-arterial chemotherapy followed by ART. Subsequently, she successfully became pregnant and gave birth.

Case

The patient was a 22-year-old Japanese woman, who was single and nulligravida. Her chief complaint was abnormal genital bleeding. She visited a local clinic when she noticed that there was increased vaginal discharge since February 200X, and the amount of genital bleeding had gradually increased. Pap smear revealed class V squamous cell carcinoma (SCC), and a biopsy exam revealed moderate dysplasia. Thus, she was subsequently transferred to a local hospital in March 200X. A cervical tumor with exophytic growth was detected, and the biopsy specimen revealed a potential verrucous carcinoma. Therefore, an abdominal radical hysterectomy was recommended. However, due to her young age, fertility preservation was desired, and she was recommended to our hospital.

A papillary growth cervical carcinoma measuring over 4 cm in diameter was detected upon inspection. A pelvic exam revealed that the uterus was normal in size, the bilateral adnexae were not palpable, and the bilateral parametrium was soft. A second Pap smear performed by us showed a class V SCC tumor with broad necrotic tissue and large atypical cells. Further, another biopsy revealed squamous cell carcinoma with typical warty appearance and intercellular bridges consisting of less atypical cells with broad cytoplasm. Thus, this tumor was diagnosed as verrucous carcinoma.

Analyses for tumor markers showed the following: CEA 0.8 ng/ml, CA19-9 17.2 U/ml, CA125 12 U/ml, CYFRA 1.1 ng/ml, NSE 6.7 ng/ml, and SCC 4.6 ng/ml. Human papillomavirus (HPV) type 31 was also detected.

A pelvic MRI showed the presence of a uterine cervical tumor with exophytic growth (Fig. 1).

Although this case was a stage Ib2 bulky cervical carcinoma, tumor histology was well-differentiated and stromal invasion seemed shallow. Based on this diagnosis, intra-arterial neoadjuvant chemotherapy (IANAC) was performed followed by surgery. The chemotherapy regimen included cisplatin (CDDP) 100 mg/body and mitomycin C (MMC) 10 mg/body administered by insertion of the catheter into the right femoral artery and placement of the catheter tip into the bilateral internal iliac artery. Bolus infusions at half dose were given to the left and right internal iliac arteries (Park et al., 1995).

IANAC was initially administered on March 22, 200X. Two weeks later, an obvious shrinkage of the tumor was observed. Tumor diameter had decreased to approximately 2 cm. A second course of IANAC was administered on April 12, 200X, and two weeks later, the tumor could no longer be observed by the naked eye (Fig. 2). An MRI performed on April 27, 200X showed that the residual tumor measured 12×9×6 mm in size. No severe adverse effects of IANAC were observed. The level of SCC Ag declined from 4.6 ng/ml to 0.9 ng/ml.

Fertility-sparing surgery was considered, and ART was performed on May 2, 200X. Bilateral uterine arteries and pelvic nerve were

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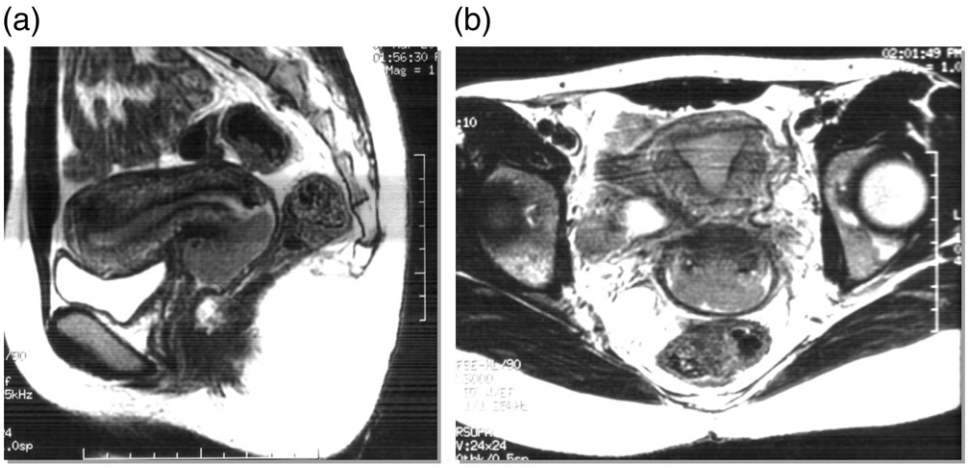

Fig. 1. A pelvic MRI showing the presence of a uterine cervical tumor with exophytic growth, measuring 46×42×12 mm, that was mainly located on the anterior cervical lip, but tumor invasion seemed shallow (a), and parametrium invasion and pelvic lymphadenopathy were not detected (b).

preserved. No apparent swollen pelvic lymph nodes were observed upon dissection, and a negative endocervical cut end was shown by frozen histological diagnosis. ART was successfully completed, and a cervical cerclage with polydioxanone (PDS) suture was placed. Operation time was 5 h and 21 min, and blood loss was 436 ml.

The excised specimen included only a tiny papillary tumor. The final pathological diagnosis was a microinvasive well-differentiated squamous cell carcinoma with no pelvic lymph node metastasis.

No adjuvant treatment was needed, and she was placed under our observation.

This patient married on May, 200X+1. After marriage, she tried to conceive, but she experienced difficulties. Beginning on May, 200X+2, artificial insemination by the husband was performed 5 times, but she failed to get pregnant. Then, on May, 200X+4, she received in vitro fertilization and embryo transfer (IVF–ET), and she finally conceived.

After conception, she was admitted to our hospital at 10 weeks of gestation for bed rest. Cervical cerclage with nylon suture was performed at 12 weeks and 2 days of gestation. From around 16 weeks of gestation, a small amount of genital bleeding began; thus, absolute bed rest was instructed. The fetus was in the vertex presentation, and rupture of the membrane occurred at 27 weeks and 6 days. Thus, an emergency Cesarean section was performed at 28 weeks of gestation. The immature male baby was born, weighing 1258 g, and had Apgar scores of 5 at 1 min and 6 at 5 min. The post-operative course was mostly uneventful. Five years and four months after the trachelectomy, she has been alive without disease and her child has been growing favorably.

Discussion

This is the world's first case of a patient treated with neoadjuvant chemotherapy for bulky cervical cancer of stage Ib2 followed by ART, who subsequently conceived and gave birth successfully.

VRT is limited by the resectable size of the parametrium from the uterine cervix because of the narrowness of the vagina (Einstein et al., 2009). However, for the cases with large tumors (2–4 cm), several reports describing the use of VRT after neoadjuvant chemotherapy (NAC) have emerged in recent years (Marchiole et al., 2011; Gottschalk et al., 2011). Tsubamoto et al. (2012) reported a case series, where 3 patients with stage Ib bulky cervical carcinoma underwent simple vaginal trachelectomy and abdominal lymphadenectomy with resection of paracervical tissues after NAC. However, no pregnancies were sought among them.

Recently, Abu-Rustum et al. (2008) performed ART for cancer patients with stage Ib1. Although the majority of their patients underwent successful surgery, nearly 32% required hysterectomy or postoperative chemoradiation for oncologic reasons. Thus, about one third of the stage Ib1 patients treated by ART had risk factors that required adjuvant therapy after surgery.

Nishio et al. (2009) performed ART for 61 patients. There were six recurrences (9.8%), none of which occurred in patients with tumors

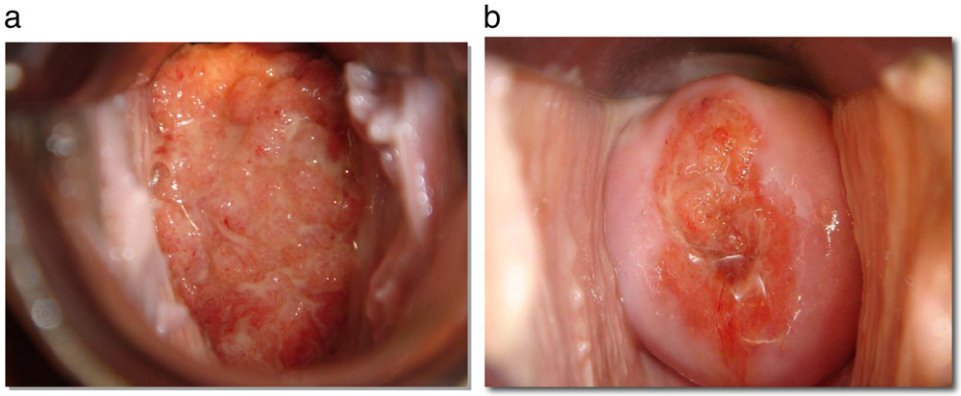

Fig. 2. A papillary growth cervical carcinoma, measuring over 4 cm in diameter, was detected (a). After a second course of IANAC, the tumor could no longer be observed by the naked eye (b).

<2 cm except in one case with adenocarcinoma. Thus, ART is recommended for patients with a tumor diameter of <2 cm. In Japan, nerve sparing radical hysterectomy has been widely utilized since the radicality of this procedure seems to be less than the conventional one. However, Nishio et al. did not include details about its indications and extent of the nerve sparing procedure. If preoperative imaging is able to accurately confirm shallow stromal invasion and no lymph node metastasis, and excessive nerve sparing is not utilized, then ART can be performed more safely with higher curative rates.

In 2011, Lukas et al. (2011) reviewed the performance of ART in Ib1 tumors larger than 2 cm. There was a higher risk of extrauterine spread and the risk of recurrence was significantly higher. However, their review mainly discussed results from 3 papers, one of which was by Nishio et al in 2009 as mentioned above while the other two are relatively old and thus may not be applicable to the current situation. In contrast, Li et al. (2011) performed ART for 62 patients, 14 of 36 Ib1 cases had tumors >2 cm, and no recurrences were observed at a median follow-up of 22.8 months.

Cancer treatment with fertility preservation is an important alternative option especially among younger patients with small tumors. But regardless of the tumor size, radical trachelectomy should be performed only when the patient adequately understands the many pregnancy-related risks after surgery, for example premature birth, and truly desires it.

In this report, a patient with bulky cervical cancer stage Ib2 was diagnosed carefully with regard to histology, depth of invasion and tumor spread. NAC was administered, thereby fertility preservation and radicality were sustained. After a 5-year follow-up period, there is no evidence of disease, and the child has shown no adverse effects of treatment. This case is the first case of successful pregnancy and delivery after NAC and abdominal radical trachelectomy. This report may bear great significance and provide useful information towards treatment of young cervical cancer patients especially with respect to fertility preservation.

Conflict of interest statement
All authors declare that there are no conflicts of interest.

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